



HEALTH ZONE

AAEP Convention

Top Equine Studies of 2014

BY ALEXANDRA BECKSTETT, ERICA LARSON, AND DR. NANCY LOVING

To kick-start the convention's educational sessions, three veterinarians presented their favorite studies from the past year to their peers. Dr. Lisa Fortier, (on the right in the image below) professor of Large Animal Surgery at Cornell University, in Ithaca, N.Y., shared lameness and surgery picks; Dr. Carol Clark, (center) of Peterson & Smith Equine Hospital, in Ocala, Fla., presented medicine studies; and Dr. Terry Blanchard, (left) theriogenology professor and researcher at Texas A&M University, in College Station, tackled reproduction topics.

Stem Cells for Treating Stifle Lesions

Fortier began by describing a "landmark paper" evaluating the outcome of horses with meniscal, cartilage, or ligamentous stifle lesions treated with a combination of surgery and intra-articular (in the joint) mesenchymal

stem cells (MSCs) and hyaluronic acid injections. She said 44% of all horses returned to work following treatment; of those, 75% with meniscal disease returned to work (compared to 60% of control horses). Her take-home was that MSCs appeared to benefit meniscal lesion cases.

Nerve Block Variability

Next, she described two studies on blocks for the deep branch of the lateral plantar nerve, used to diagnose hind limb suspensory desmitis (inflammation of the ligament). There's a high degree of variability with these blocks, Fortier said; high-volume injections diffused more than low, and analgesia traveled up to 2 cm above and up to 5 cm below the injection site. Additionally, 37% of horses had evidence of analgesia in the tarsal sheath, and 24% of horses in the tarso-metatarsal joint (a low-motion hock joint).

The take-home? Blocks aren't specific. So, if the horse responds favorably, use diagnostic imaging to see what's going on.



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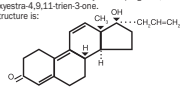

CYTOWAVE
EQUINE THERAPY

Regu-Mate® (altrenogest)

Solution 0.22% (2.2 mg/mL)

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION: Regu-Mate® (altrenogest) Solution 0.22% contains the active synthetic progestin, altrenogest. The chemical name is 17 α -allyl-17 β -hydroxyestra-4,9,11-trien-3-one. The CAS Registry Number is 850-52-2. The chemical structure is:



Each mL of Regu-Mate® (altrenogest) Solution 0.22% contains 2.2 mg of altrenogest in an oil solution.

ACTIONS: Regu-Mate® (altrenogest) Solution 0.22% produces a progestational effect in mares.

INDICATIONS: Regu-Mate® (altrenogest) Solution 0.22% is indicated to suppress estrus in mares. Suppression of estrus allows for a predictable occurrence of estrus following drug withdrawal. This facilitates the attainment of regular cyclicity during the transition from winter anestrus to the physiological breeding season. Suppression of estrus will facilitate management of prolonged estrus conditions. Suppression of estrus may be used to facilitate scheduled breeding during the physiological breeding season.

CONTRAINDICATIONS: Regu-Mate® (altrenogest) Solution 0.22% is contraindicated for use in mares having a previous or current history of uterine inflammation (i.e., acute, subacute, or chronic endometritis). Natural or synthetic estrogen therapy may exacerbate existing low-grade or "smoldering" uterine inflammation into a fulminating uterine infection in some instances.

PRECAUTIONS: Various synthetic progestins, including altrenogest, when administered to rats during the embryonic stage of pregnancy at doses manyfold greater than the recommended equine dose caused fetal anomalies, specifically masculinization of the female genitalia.

DOSEAGE AND ADMINISTRATION: While wearing protective gloves, remove shipping cap and seal; replace with endosed plastic dispenser. Remove cover from bottle dispensing tip and connect laser syringe (without needle). Draw out appropriate volume of Regu-Mate solution. (Note: Do not remove syringe while bottle is inverted as spillage may result.) Detach syringe and administer solution orally at the rate of 1 mL per 110 pounds body weight (0.04 mg/kg) once daily for 15 consecutive days. Administer solution directly on the base of the mare's tongue or on the mare's usual grain ration. Replace cover on bottle dispensing tip to prevent leakage. Excessive use of a syringe may cause the syringe to stick; therefore, replace syringe as necessary.

WHICH MARES WILL RESPOND TO REGU-MATE® (altrenogest) SOLUTION 0.22%: Extensive clinical trials have demonstrated that estrus will be suppressed in approximately 95% of the mares within three days; however, the post-treatment response depended on the level of ovarian activity when treatment was initiated. Estrus in mares exhibiting regular estrus cycles during the breeding season will be suppressed during treatment; these mares return to estrus four to five days following treatment and continue to cycle normally. Mares with small follicles continued in anestrus and failed to exhibit normal estrus following withdrawal.

Response in mares in the transition phase between winter anestrus and the summer breeding season depended on the degree of follicular activity. Mares with inactive ovaries and small follicles failed to respond with normal cycles post-treatment, whereas a higher proportion of mares with ovarian follicles 20 mm or greater in diameter exhibited normal estrus cycles post-treatment. Regu-Mate® (altrenogest) Solution 0.22% was very effective for suppressing the prolonged estrus behavior frequently observed in mares during the transition period (February, March and April). In addition, a high proportion of these mares responded with regular estrus cycles post-treatment.

SPECIFIC USES FOR REGU-MATE® (altrenogest) SOLUTION 0.22%:

SUPPRESSION OF ESTRUS TO:

1. Facilitate attainment of regular cycles during the transition period from winter anestrus to the physiological breeding season. To facilitate attainment of regular cycles during the transition phase, mares should be examined to determine the degree of ovarian activity. Estrus in mares with inactive ovaries (no follicles greater than 20 mm in diameter) will be suppressed but these mares may not begin regular cycles following treatment. However, mares with active ovaries (follicles greater than 20 mm in diameter) frequently respond with regular post-treatment estrus cycles.

DOSEAGE CHART:	
Approximate Weight in Pounds	Dose in mL
770	7
880	8
990	9
1100	10
1210	11
1320	12

2. Facilitate management of the mare exhibiting prolonged estrus during the transition period. Estrus will be suppressed in mares exhibiting prolonged behavioral estrus either early or late during the transition period. Again, the post-treatment response depends on the level of ovarian activity. The mares with greater ovarian activity initiate regular cycles and conceive sooner than the inactive mares. Regu-Mate® (altrenogest) Solution 0.22% may be administered early in the transition period to suppress estrus in mares with inactive ovaries to aid in the management of these mares or to mares later in the transition period with active ovaries to prepare and schedule the mare for breeding.

3. Permit scheduled breeding of mares during the physiological breeding season. To permit scheduled breeding, mares which are regularly cycling or which have active ovaries should be given Regu-Mate® (altrenogest) Solution 0.22% daily for 15 consecutive days beginning 20 days before the date of the planned estrus. Ovulation will occur 5 to 7 days following the onset of estrus as expected for untreated mares. Breeding should follow usual procedures for mares in estrus. Mares may be regulated and scheduled either individually or in groups.

ADDITIONAL INFORMATION: A 3-year well controlled reproductive safety study was conducted in 27 pregnant mares, and compared with 24 untreated control mares. Treated mares received 2 mL Regu-Mate® (altrenogest) Solution 0.22% 150 body weight (2x dosage recommended for estrus suppression) from day 20 to day 325 of gestation. This study provided the following data:

- In fly offspring (all ages) of treated mares, clitoral size was increased.
- Fly offspring from treated mares had shorter intervals from Feb. 1 to first ovulation than flies from their untreated mare counterparts.
- There were no significant differences in reproductive performance between treated and untreated animals (mares & their respective offspring) measuring the following parameters:
 - mean interval from first to second cycle and second to third cycle, mares only.
 - interval from Feb. 1 to first ovulation, in mares only.
 - mean interval from first to second cycle and second to third cycle, mares only.
 - follicle size, mares only.
 - at 50 days gestation, pregnancy rate in treated mares was 81.8% (9/11) and untreated mares was 100% (4/4).
 - after 3 cycles, 11/12 treated mares were pregnant (91.7%) and 4/4 untreated mares were pregnant (100%).
 - colt offspring of treated and control mares reached puberty at approximately the same age (52 & 54 weeks respectively).
 - stallion offspring from treated and control mares showed no differences in seminal volume, spermatozoal concentration, spermatozoal motility, and total sperm per ejaculate.
 - stallion offspring from treated and control mares showed no differences in sexual behavior.
 - testicular characteristics (scrotal width, testis weight, parenchymal weight, epididymal weight and height, testicular height, width & length) were the same between stallion offspring of treated and control mares.

REFERENCES:

Shoemaker, C.F., E.L. Squires, and R.K. Shidler, 1989 Safety of Altrenogest in Pregnant Mares and on Health and Development of Offspring. Eq. Vet. Sci. (9): No. 2: 69-72.
Squires, E.L., R.K. Shidler, and A.O. McKinnon, 1989 Reproductive Performance of Offspring from Mares Administered Altrenogest During Gestation. Eq. Vet. Sci. (9): No. 2: 73-76.

WARNING: Do not use in horses intended for food.

HUMAN WARNINGS: Skin contact must be avoided as Regu-Mate® (altrenogest) Solution 0.22% is readily absorbed through unbroken skin. Protective gloves must be worn by all persons handling this product. Pregnant women or women who suspect they are pregnant should not handle Regu-Mate® (altrenogest) Solution 0.22%. Women of child bearing age should exercise extreme caution when handling this product. Accidental absorption could lead to a disruption of the menstrual cycle or prolongation of pregnancy. Direct contact with the skin should therefore be avoided. Accidental spillage on the skin should be washed off immediately with soap and water.

INFORMATION FOR HANDLERS:

WARNING: Regu-Mate® (altrenogest) Solution 0.22% is readily absorbed by the skin. Skin contact must be avoided; protective gloves must be worn when handling this product.

Effects of Overexposure: There has been no human use of this specific product. The information contained in this section is extrapolated from data available on other products of the same pharmacological class that have been used in humans. Effects anticipated are due to the progestational activity of altrenogest. Acute effects after a single exposure are possible; however, continued daily exposure has the potential for more untoward effects such as disruption of the menstrual cycle, uterine or abdominal cramping, increased or decreased uterine bleeding, prolongation of pregnancy and headaches. The oil base may also cause complications if swallowed. In addition, the list of people who should not handle this product (see below) is based upon the known effects of progestins used in humans on a chronic basis.

PEOPLE WHO SHOULD NOT HANDLE THIS PRODUCT:

- Women who are or suspect they are pregnant.
- Anyone with thrombophlebitis or thromboembolic disorders or with a history of these events.
- Anyone with cerebral-vascular or coronary artery disease.
- Women with known or suspected carcinoma of the breast.
- People with known or suspected estrogen-dependent neoplasia.
- Women with undiagnosed vaginal bleeding.
- People with benign or malignant tumors which developed during the use of oral contraceptives or other estrogen-containing products.
- Anyone with liver dysfunction or disease.

ACCIDENTAL EXPOSURE: Altrenogest is readily absorbed from contact with the skin. In addition, the oil based product can penetrate porous gloves. Altrenogest should not penetrate intact rubber or impervious gloves; however, if there is leakage (i.e., pinhole, spillage, etc.), the contaminated area covered by such occlusive materials may have increased absorption. The following measures are recommended in case of accidental exposure:
Skin Exposure: Wash immediately with soap and water.
Eye Exposure: Immediately flush with plenty of water for 15 minutes. Get medical attention.
Eye Exposure: Do not induce vomiting. Regu-Mate® (altrenogest) Solution 0.22% contains an oil. Call a physician. Vomiting should be supervised by a physician because of possible pulmonary damage via aspiration of the oil base. If possible, bring the container and labeling to the physician.

CAUTION: For oral use in horses only. Keep this and all medication out of the reach of children.

Store at or below 25°C (77°F).

NADA# 131-310. Approved by FDA.

HOW SUPPLIED:

Regu-Mate® (altrenogest) Solution 0.22% (2.2 mg/mL).

Each mL contains 2.2 mg altrenogest in an oil solution.

Available in 1000 mL plastic bottles.

* US Patents 3,453,267; 3,478,067; 3,484,462

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HEALTH ZONE

AAEP Convention

CT to Assess Hock Lameness

Next, Fortier described a paper in which scientists retrospectively evaluated CT findings in horses with tarsal lameness. They found a variety of pathologies within the hock, Fortier said, some of which weren't visible on other imaging modalities. Thus, she encouraged practitioners to seek further diagnostic information via a 3-D modality (like CT or MRI) if radiographs and/or ultrasound appear clean in a horse exhibiting hock lameness.

Abnormal Breathing Patterns and Respiratory Disease

Changing gears, Fortier described a study in which researchers evaluated whether abnormal breathing patterns at the canter and gallop are associated with respiratory tract disease. They studied 365 horses referred for evaluation due to poor performance or an upper respiratory tract obstruction.

The frequency of abnormal breathing patterns decreased as speed increased. Also, horses with a 2:1 pattern (taking one breath over two strides instead of one breath per stride) at higher speeds were more likely to have upper respi-

ratory tract disease, while horses with abnormalities at lower speeds could have either upper or lower respiratory tract disease.

Fortier's take-home: While not every horse with an airway obstruction will have a 2:1 breathing pattern, all affected horses warrant further upper and lower respiratory tract investigation.

Ophthalmology Studies

Clark began her medicine synopsis by describing several papers on eye problems. The first was on treating corneal stromal abscesses with 5% voriconazole (an antifungal) solution by injecting the drug immediately adjacent to the anterior stroma rather than directly into the abscess, as veterinarians more typically do. Necessary treatment time decreased from the reported average of eight weeks down to 5.5 weeks and resulted in less scarring.

Next, Clark reviewed a retrospective (2006-13) study of 18 cases of orbital (surrounding the eye) fractures. In more than half of the cases, the researchers noted comminuted fractures (tiny bone fragments). They also noted that epistaxis (nosebleed) likely indicates sinus

EFFECTIVE TREATMENT FOR SUSPENSORY LIGAMENT INJURIES

One of the hot topics during the AAEP event in Utah was the lack of technologies that address the complexities of equine suspensory injuries.

"We were surprised how often we overheard someone talking about suspensories and they were not aware of effective modalities out there," said Elaine Sniatynsky, National Sales Manager for Cytowave.

And other than using a scattershot approach, there aren't any effective singular treatments for horses' suspensory injuries.

Richard Parker, the inventor of Cytowave, said the reason for the confusion was simple.

"Adequate therapies for suspensory injuries are lacking because they do not address the true nature of the injury and, therefore, yield unreliable results."

Suspensory injuries are among the

most troublesome to treat, and it is due to their complex nature. The racing world knows this as well as any other discipline out there.

Parker added, "Cytowave's chief benefit is to reliably accelerate and improve the quality of the recovery for suspensory injuries by supplying an amplified natural repair signal specific to the bone attachment point, minor muscle tissue involvement, and ligament tissue itself. The horse's cellular mechanics recognize and adopt these independent signals and consequently accelerate and improve tissue repair."

Most individuals in the industry have been waiting for an effective, reliable, non-invasive treatment for suspensory injuries. Given that veterinarians, trainers, and owners have used Cytowave to treat a number of suspensory injuries successfully, that time is now.

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ANNE M. EBERHARDT

When topical eye medications are applied, there is always a concern that it could stimulate bacterial growth

involvement. In addition, they identified neurologic signs in a horse that had reared in a confined space and suffered traumatic brain injury. In general, they were fairly successful in treating all cases, with nearly 87% returning to previous function and 60% with good cosmetic appearance.

Then Clark presented a paper in which veterinarians evaluated the use of cyclosporine implants to control immune-mediated keratitis (corneal inflammation). The researchers placed two to four of these silicone implants into 20 eyes and determined that it helped effectively control superficial (near the surface) and endothelial (the inner layer of the cornea) forms of keratitis, and the horses came off all or all but one topical medication through the follow-up of 14-18 months.

When applying any topical eye medication, there is always a concern that it could stimulate bacterial growth, thereby complicating the case. Clark described a study that showed no difference in bacterial growth in the eye with or without topical anesthetic tetracaine treatment.

Respiratory Conditions

Clark reviewed a paper in which the authors evaluated the correlation between airborne particulates and tracheal mucus at a Thoroughbred racetrack. If there is sufficient mucus in the respiratory tract, a horse experiences exercise compromise due to inflammation—the higher the mucous score, the greater the number of inflammatory cells. Of 649 study horses, 23% had mucous scores high enough to affect performance. The researchers found particulate contamination within a horse's rebreathing zone (the 2-foot area directly around the muzzle and face) was higher in stalls during the evening hours. They suggested implementing management practices that reduce ambient particulates in the stall and barn, such as improved ventilation and dust control.

Clark also summarized the effects of environmental exposure on airway inflammation in 49 Thoroughbreds during their first month of training. The researchers measured horses' exposure to particulates, endotoxin, and ammonia and com-

Researchers suggest implementing management practices that reduce ambient particulates in the stall and barn such as improved ventilation and dust control

pared it to what they found on airway cytology (cell study). Particulates and airway inflammation especially increased with haynet use. Increased eosinophil (a type of white blood cell) numbers on cytology suggested allergic hypersensitivity related to environmental factors, the researchers concluded. Of the horses with increased eosinophil counts, 72-81% had some form of inflammatory airway disease (IAD) during the study.

In another study, researchers examined omega-3 fatty acid supplementation coupled with a low-dust diet to manage chronic lower airway inflammation. They determined that the best way to reduce airway inflammation is to remove hay; this led to 65% reduction in abnormal airway signs. Combining environmental control strategies with omega-3 fatty acid supplementation offered more benefits.

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Heart Problems in Athletic Horses

Clark reported that the American College of Veterinary Internal Medicine and European College of Veterinary Internal Medicine have prepared a consensus statement on how to diagnose and manage cardiac murmurs and arrhythmias. “The majority of horses with cardiovascular abnormalities can have some athletic use,” she said. “Periodic re-evaluations are important as many conditions are progressive.” She said a horse should not engage in athletic activities if veterinarians find evidence of pulmonary hypertension (abnormally high blood pressure in the arteries of the lungs); congestive heart failure (end-stage heart damage); or complex ventricular abnormalities (which alter the heart’s strength and/or rhythm).



ANNE M. EBERHARDT

The majority of horses with cardiovascular abnormalities can have some athletic use

Stem Cells to Treat Endometritis

Colorado State University researchers set out to determine whether biological treatments, such as autologous conditioned serum (ACS) and MSCs, could help modulate the inciting inflammatory response in mares with persistent mating-induced endometritis. They determined that both treatments decreased inflammatory response six hours post-insemination. They also found that MSCs increased the inflammatory mediator IL-1Ra, which Blanchard said might be very important in helping to control some of the effects of interleukin-1, a common pro-inflammatory cytokine produced during post-mating endometritis. Overall, they concluded that stem cells might benefit these cases.

CCFA as an Endometritis Treatment

In this experimental study, Colorado State University researchers evaluated ceftiofur crystalline free acid (CCFA) levels in the endometrium after intramuscular administration. They gave the antibiotic—normally used for lower respiratory infections—to three groups of mares (at a 6.6 mg/kg body weight dose) at various intervals and collected blood and endometrial biopsy samples. Upon analyzing these, the team determined that CCFA remains at endometrial levels above the minimum concentration for inhibiting the growth of *Streptococcus zooepidemicus*, the most common cause of infectious endometritis, for up to six days.

PRP's Effects on Endometritis

In an effort to provide veterinarians with another treatment option for persistent endometritis, researchers evaluated autologous (derived from the horse’s own blood) platelet-rich plasma’s (PRP) effects on uterine inflammatory response when infused into the uterus after artificial insemination (a common cause of inflammation that can inhibit fertility). The

team found that in susceptible mares, uterine fluid, nitric oxide levels, and percentage of neutrophils (the most abundant type of white blood cell) all decreased after PRP was administered four hours post-breeding. These measurements indicate a reduced inflammatory response, leading Blanchard to conclude that PRP might provide another effective treatment option for this condition. **BH**

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